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ABSTRACT

The American Society of Human Genetics (ASHG) recommends that testing for adult onset conditions be deferred until adulthood because of the potential for psychological harm combined with lack of medical utility. ASHG's 2016 DNA Day Essay Contest asked 9-12th graders to defend or refute this position. 1241 essays were submitted. 572 students defended ASHG's position statement, while 554 argued against. Essays that addressed Alzheimer's disease (AD) and BRCA-related Hereditary Breast and Ovarian Cancer syndrome were qualitatively analyzed for themes related to the argued position. 64.4% of students argued for deferred testing of AD, and 46.1% of students argued for deferred testing of BRCA. Relevant themes include the availability or lack of medical intervention, potential psychological benefit or consequence, and genetic testing variability and uncertain predictability. This data suggests that minors have thoughtful and insightful opinions that should be taken into consideration when considering predictive genetic testing.

KEYWORDS: Predictive testing, presymptomatic testing, minors, adolescents, adult onset, ASHG, ethics, perspectives, attitudes, genetic testing

INTRODUCTION

The introduction of genetic testing into clinical care has brought with it many obvious benefits, but also a great deal of uncertainty. In particular, it has raised ethical concerns about the potential downsides of predictive information. Predictive testing, done in the absence of any sign or symptom of disease, requires considerable forethought. While testing for adult onset disorders is accepted as a reasonable option for adults who wish to know their risk for late-onset conditions, a cautious approach is taken when considering predictive testing for children and adolescents. Disputes arise when clinicians, families, or minors themselves

consider testing for adult onset conditions before symptoms present and when there is no impact on medical care before adulthood.

Scientists are increasingly identifying genes and other biological markers that can provide presymptomatic and predictive risk estimates for developing an adult onset disorder (Roberts, Cupples, Relkin, Whitehouse, & Green, 2005). Two common examples of adult onset disorders are Alzheimer's disease (AD) and Hereditary Breast and Ovarian Cancer Syndrome (HBOC). AD is a degenerative brain disorder that causes behavioral problems and gradual loss of memory. The common form of this disease usually presents in people over 65; however, there is a genetic variant that causes the onset of disease earlier in adulthood. Finding that one carried this variant would indicate a predisposition to potentially developing symptoms much earlier in life. HBOC is a syndrome most commonly caused by a mutation in the BRCA1 gene or BRCA2 gene that results in a dramatically increased lifetime risk of developing breast and/or ovarian cancer.

The debate surrounding presymptomatic testing in minors is complex. The most widely accepted ethical justification for genetic testing of minors is the direct benefit of medical intervention or preventative measures (Borry, Stultiens, Nys, Cassiman, & Dierickx, 2006). In addition, minors and their families may choose to be tested to alleviate uncertainty or to develop a long-term plan for the future. Commonly cited reasons to avoid testing are fear that this information could create social, emotional, psychological, and educational consequences for minors (Borry, et. al., 2006). Because of these and additional concerns, clinical guidelines and position papers often discourage presymptomatic and predictive testing in minors, including guidelines from the American Society of Human Genetics (ASHG), the National Society of Genetic Counselors (NSGC), and the American Academy

of Pediatric (AAP). Guidelines typically emphasize that the age of testing should be flexible, but that genetic testing should be deferred to ensure that adolescents are competent enough to make an informed decision (Borry, et. al., 2006).

For clarity, this paper uses the words "adolescent," "minor," "student," and "young person" interchangeably as all-encompassing terms for a high school-aged person, ages 14-18.

Arguments Against Predictive Testing of Minors

Reasons to support the deferral of genetic testing until the age of 18 are considered extensively throughout the literature. Several studies that have looked at the consequences of predictive testing in adolescents assert that the disadvantages are mainly psychological in nature (Bradbury, Patrick-Miller, Ibe, Cummings, Olopade, & Daugherty, 2008). Potential psychological consequences that individuals have experienced with early testing are cited across studies, including increased disease-related stress and anxiety, distortion of family relationships, interference with normal development of self-concept, and feelings of unworthiness (Bradbury, et. al., 2008). Additionally, a positive test result has been reported to cause a loss of self-esteem, stigmatization, and lowered expectations within the family if parents limit horizons for gene-positive minors, resulting in adolescent loss of self-worth (Wertz, Fanos, & Reily, 1994).

Another argument against the genetic testing of minors is that it compromises what is often referred to as an "open future." The right to an open future is an argument based on autonomy, and suggests that the minor's right to make decisions for him or herself as an adult should be preserved to the greatest extent possible (Bredenoord, de Vries, & van Delden, 2014). This "open future" argument asserts that people have different concepts of

what a "good life" entails and have differing opinions about the pros and cons of genetic testing—therefore, individuals should be able to make their own choices according to their own values, and not have those decisions curtailed by parental or other forms of surrogate decision making (Bredenoord, et. al., 2014).

Arguments in Favor of Predictive Testing of Minors

There is a growing need to understand the psychological consequences of predictive testing (Michie, Bobrow, & Marteau, 2001). The main argument in support of testing adolescents for adult onset disorders is that testing has the potential to impact behaviors that will affect their future health (Bradbury, et. al., 2008). Many practitioners believe that some adolescents are not only equipped to handle the information, but are also able to take the information and act upon it. By engaging in healthy behaviors or starting early surveillance and management, studies suggest that they may be able to decrease or postpone their risk of developing symptoms of the disease (Aatre & Day, 2011). Some medical professionals believe that in certain instances, minors will indeed benefit psychologically from the information, giving them both relief of having identified their condition early and a feeling of control (Aatre & Day, 2011). Although there is a concern that predictive testing in unaffected minors could induce unnecessary anxiety and distress, some data actually suggests the opposite, revealing that testing can provide reassurance, lessen uncertainty, and promote a healthy sense of control (Aarte & Day, 2011).

Further, some experts have proposed that genetic testing can have a positive effect on relationships, decrease anxiety and depression, and encourage open communication. Through such communication, gene-positive minors have the ability to become active participants in their health. This may help to reduce stigmatization and ease requests for help if needed in

the future (Duncan & Delatycki, 2006; Mand, Gillam, Delatycki, & Duncan, 2012). Withholding genetic information may squander the opportunity for a young person to take ownership of their genetic status and incorporate it as part of their identity (Anderson, Hayeems, Shuman, Szego, Monfared, Bowdin, & Meyn, 2015).

Another proposed reason to allow predictive genetic testing at a younger age is for planning purposes. Early testing allows for parents to properly prepare for their child's future, and allows children time to adjust while still having the oversight and support of their parents (Rhodes, 2006). A review of studies described that both healthcare professionals and young adults recognized that family and reproductive planning is quickly approaching at the time of testing. In order to proactively prepare for one's future, young adults consider it beneficial and necessary to go through the process of predictive genetic testing (Mand, et. al., 2012).

Current Research on Predictive Testing in Adults and Adolescents

While there have been many studies on the emotional impact of genetic testing on adults, much less is known about the impact on children and adolescents, who are often deemed more "vulnerable to emotional distress" than adults (Michie, et. al., 2001).

In one influential study called the REVEAL (Risk Evaluation and Education for Alzheimer's Disease) study performed by Roberts, Cupples, Relkin, Whitehouse, and Green (2005), 162 adults with a family history of AD were randomly assigned to the disclosure of results group or the nondisclosure of results group. The final analysis suggested that risk assessment and genotype disclosure did not adversely affect the psychological wellbeing of the adults in the study. In fact, following risk disclosure, 90% of all participants reported the same or lower anxiety regarding their risk of developing AD compared with baseline levels.

However, the participants with negative results were more likely to report lower levels of anxiety. In addition, there was an increase in preventative lifestyle changes in the group that tested positive for the high risk allele, APOE4. This study suggests that psychological outcomes can be neutral in regard to pre-symptomatic testing, and that some patients will actually take the preventative measures despite the overwhelming information.

In one of the few studies that examined the emotional impact of predictive genetic testing on minors, Michie, Bobrow, and Marteau (2001) focused on individuals tested for familial adenomatous polyposis (FAP). The study's main objective was to determine if minors aged 10-16 or adults who received positive results following predictive testing for FAP experienced significant levels of anxiety or depression. The 10-16 year-olds who received positive results were slightly more anxious and depressed than those who received negative results. However, the minors receiving positive or negative results did not show higher levels of anxiety or depression than adults in comparable circumstances.

Testing Recommendations in the United States

The development of technologies that can test asymptomatic minors for adult onset diseases creates a number of ethical and legal issues (American Society of Human Genetics & American College of Medical Genetics, 1995). To facilitate agreement on the points of contention surrounding these issues, ASHG and the American College of Medical Genetics and Genomics (ACMG) jointly released a statement regarding the testing of minors in 1995 (ASHG & ACMG, 1995). This publication was influential in guiding clinicians and families during a time in which numerous genetic tests were introduced, particularly presymptomatic and predictive tests (Botkin, Belmont, Berg, Berkman, Bombard, Holm, Levy, Ormond, Saal, Spinner, Wilfond, & McInerney, 2015).

As knowledge of genetics and genomics continued to grow, so did the public interest in issues related to genetic testing and the expanded use of this type of testing (Friedman Ross, Saal, David, & Anderson, 2013). As a result, the topic of testing minors was revisited in 2015, when ASHG released an independent position statement. A new statement was deemed appropriate, given the evolution of testing combined with the mounting questions and concerns raised in regards to testing minors (Botkin, et. al., 2015).

The 2015 ASHG statement recommends that unless there is an available and appropriate clinical intervention during childhood, predictive or presymptomatic testing for adult onset conditions should be deferred at minimum until the minor is a consenting adult who can participate in medical decision making (Botkin, et. al., 2015). However, ASHG recommends that providers acknowledge that in some cases, testing might be reasonable after thorough consideration and clinical evaluation. In some circumstances, facilitating predictive testing for a minor may be justified. For example, if it can alleviate significant psychosocial stress within a family or ease life-planning decisions, then testing may be justifiable. Botkin, et. al. (2015) noted that empirical research on the psychosocial impact of predictive and presymptomatic testing is limited and suggested that more research is necessary for future policy recommendations.

In February of 2017, the National Society of Genetic Counselors (NSGC) updated its position statement regarding the genetic testing of minors for adult onset conditions. NSGC briefly states that the deferral of predictive testing of minors is preferable, and optimally should be deferred when the results will not impact childhood medical decisions or management. They also encourage deferring this type of testing until the minor has the "capacity" to consider the risks, benefits, and limitations of such testing. NSGC states,

"his/her circumstances, preferences, and beliefs [should be taken] into account to preserve his/her autonomy and right to an open future" (NSGC, 2017).

The American Academy of Pediatrics (AAP) also recommends deferring predictive testing until adulthood "unless an intervention initiated in childhood may reduce morbidity or mortality." They also add as an exception to this recommendation that testing may be deemed appropriate for a family experiencing "significant psychosocial burden" (AAP Policy Statement, 2013).

Testing Recommendations in Foreign Countries

In general, similar points have been made by genetic societies worldwide that have taken a stance on the predictive testing of minors. In Canada, the Canadian Paediatric Society (CPS) states that, ideally, the decision to test should be made with the minor, when he/she is competent enough to make the decision (CPS, 2003). Though CPS believes that adolescents are not able to be completely autonomous in these situations, they recognize that, "it does not seem justified…to refuse testing to a fully informed, competent adolescent who is requesting [genetic testing]" (CPS, 2003).

The European Society of Human Genetics (ESHG) and the Human Genetic Society of Australasia (HGSA) have made recommendations that "the best interests of the young person must prevail" (HGSA, 2014) and the opinion of the minor should be taken into consideration "as an increasingly determining factor in proportion to his or her age or degree of maturity" (ESHG, 2009). ESHG stresses that well-informed minors with an adequate understanding of the test and its potential implications should be considered competent to make the decision for his or herself (ESHG, 2009). ESHG and HGSA suggest that predictive testing for an adult onset condition is acceptable only if there are available preventative measures that can be

taken (ESHG, 2009, HGSA, 2014).

Compared to the United States, Europe, and Canada, the age at which minors are considered autonomous is much younger in Australia. In fact, the HGSA does not recommend a specific age to differentiate between who can make an informed decision and who cannot—each request for testing requires "individual assessment" (HGSA, 2014). In Australia, adolescents are divided into immature and mature youths based on their cognitive capacity and psychosocial maturity, and are then deemed able to make fully formed decisions after a full psychosocial assessment (HGSA, 2014).

The Need for Adolescent Opinions

With the limited research focused on the predictive testing of minors, existing guidelines are based on suggestions and speculation by clinicians and bioethicists. Notably, there is a voice lacking in this discussion: the adolescents themselves. The voices of young adults continue to be scarce despite the important role their opinions play in shaping existing guidelines and practices (Duncan, Gillam, Savulescu, Williamson, Rogers, & Delatycki, 2008). Thus, the focus of our project is to unveil adolescent perspectives regarding genetic testing for adult onset conditions. More specifically, we seek to uncover how their opinions, as reflected in essays written by minors for ASHG's annual DNA Day Essay Contest, align with ASHG's position statement on genetic testing of minors.

MATERIALS & METHODS

Study Design

Essays were submitted by 9th-12th grade students (roughly ages 14-18) to ASHG's annual 2016 international DNA Day Essay Contest. Essays were thematically analyzed using

a mixed-methods approach. This analysis was used to investigate reasons why minors would defer or not defer genetic testing for adult onset disease. Demographic information including gender, grade, and submission location were also analyzed. All essays were uploaded into the qualitative analysis program Atlas. Qualitative analyses were conducted using a grounded theory approach to assess minors' views and arguments for and against testing for adult onset conditions.

Participants & Essay Question

ASHG's 2016 DNA Day essay contest question was as follows:

> Choose a genetic test that is currently available for a condition or disease that does not cause symptoms until adulthood (i.e., an adult-onset condition such as hereditary breast cancer). Describe how the test works and how certain the test results are. Then, either defend or refute the recommendation below from ASHG's recent position statement on pediatric genetic testing.
>
> > "Adolescents should be encouraged to defer predictive or pre-dispositional testing for adult-onset conditions until adulthood because of the complexity of the potential impact of the information at formative life stages."

Teachers entered essays on behalf of their students, and a total of 1241 essays were submitted. Teachers could submit essays from up to six students per class for up to three classes. Participants were informed that essays might be used for research purposes. This study received an exemption from the Sarah Lawrence College Institutional Review Board (IRB) in April 2016 along with an approval from the Geisinger Health System IRB in March 2016.

Initial Evaluation of Data

All essays were categorized by grade, sex, chosen disease, and whether or not the student chose to defer testing until adulthood. Essays that did not focus on a single disease

were titled ‘None’ in the disease category, and the essays that did not pick defer or not defer were labeled ‘Other.’ To ensure accuracy, 150 essays were randomly selected to cross-check labeling.

Once the essays were labeled and cross-checked, they were grouped into categories based on their content. The essays that were marked ‘Other’ or ‘None’ were reviewed to determine if the information could be used to identify a position regarding the testing of minors. A total of 77 essays that did not contribute valid information were discarded. Reasons for discarding None/Other essays included:

- Essay did not address essay prompt or focused on a different topic
- Essay was illegible or unintelligible
- Essay did not state an opinion
- Essay misinterpreted question/ASHG policy

Reasons for keeping None/Other essays included:

- Essay indicated personal/family/individual choice
- Essay showed an understanding of the question and represented both sides of the argument without choosing a single side

Decisions were made by consensus among all coders. Essays that were kept were uploaded to Atlas and remained in a separate category named ‘None/Other.’

Developing Codebook and Analysis Framework

To create the codebook, the three most common disorders were identified (HD, AD, & BRCA), and all essays referencing those disorders were assigned two readers. Themes and categories based on the essays’ content were identified and served as the basis for an

inductive data analysis. Lists of topics were assembled by each coder and then combined to build a holistic picture of the essays' content. Coders continued reading until a saturation point was reached when no new themes emerged. Subsequently, coders combined their findings and then integrated all themes into categories. An initial codebook was established by consensus and reviewed by an external supervisor.

The clarity of the codes was checked through an iterative process to ensure the codes were applied appropriately and consistently. To start, all investigators were given five randomly selected sentences to apply the relevant codes. The process was repeated until reviewer agreement indicated that the codes were unanimously defined. Next, once the codebook was agreed upon, five essays were assessed by each coder separately, and then compared. This process was repeated until all readers were consistently applying the same codes to the same themes found in the essays. Once inter-rater reliability (IRR) was reached, essays were divided among 4 coders to code independently. The IRR was 0.95 alpha (≥0.75 IRR), allowing the data to be analyzed in Atlas.

Codebook

The final codebook contained 25 codes (Table I.). Twenty four of the codes have a counterpart; for example, Code 1: Psychological benefit to minor is paired with Code 2: Psychological risk to minor. Each code consisted of a general category, an explanation of the themes/topics that related to that category, and example statements for when to apply the code to avoid code drift.

Code Number and Code			
1.	Psychological benefits to minor	13.	Disrupts formative years
2.	Psychological risks to minor	14.	Social risks
3.	Genetic testing variability and uncertain predictability	15.	Social benefits
4.	Genetic testing accuracy and predictability	16.	Mature and incapable
5.	Factual genetic/disorder information	17.	Immature and capable
6.	Incorrect facts	18.	Potential discrimination
7.	Risks to family	19.	Necessary to plan/prepare
8.	Benefits to family	20.	Unnecessary to plan/prepare
9.	Personal experience with the condition	21.	Advancements in science
10.	Personal experience with testing	22.	Case-by-case
11.	Medical benefit or prevention	23.	Loss of autonomy
12.	No medical benefit or prevention	24.	Individual's choice
		25.	Family/Parent's choice

Table I. The complete list of 25 codes.

Thematic Analysis (ATLAS.ti)

Of the 1241 essays submitted, 313 essays that discussed BRCA, Lynch, and Alzheimer's disease (189, 13, and 111, respectively) were thematically coded. For the

purposes of this analysis, only the essays that discussed BRCA and AD were analyzed for thematic content relating to the reasons to defer or not defer genetic testing for adult onset conditions.

RESULTS

There were 1241 student essays submitted to the ASHG DNA Day Essay Contest. The majority of submissions (87%) were from the United States while a smaller number of essays (13%) were submitted by international students. Figure 1. depicts the number of essays submitted from each US state. Six states submitted no essays. The maximum number of essays submitted was 186 (New York). Of the 44 states that participated, the average number of essay submissions was 28.

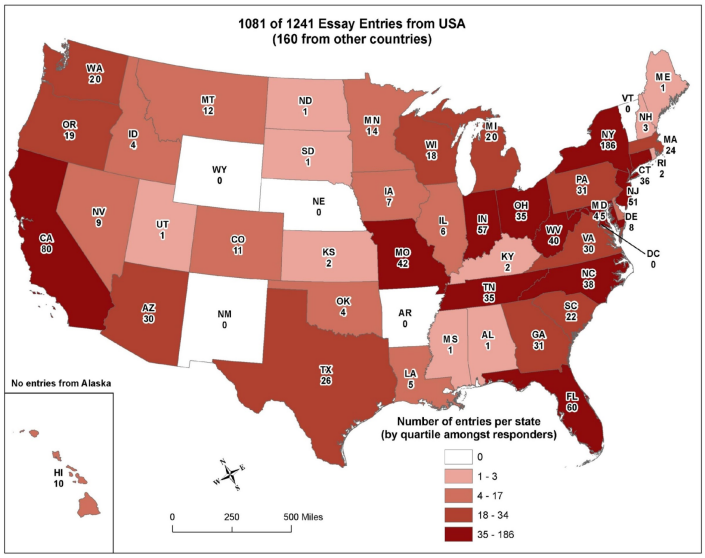

Figure 1. Map of the United States depicting the number of essay submissions. A darker color correlates with a higher number of essay submissions. White indicates no essays were submitted.

Females submitted 67% of the essays and males submitted 37%. The majority of essays (88%) were evenly distributed between grades 10-12, and 9th graders represented the remaining 12%. Over 100 conditions were discussed by the students, but 60 of them were

mentioned by only one student. The five most commonly discussed conditions are listed in Table II.

Top 5 Conditions Chosen		
HD	466	(38%)
BRCA	205	(17%)
Alzheimer's	118	(10%)
FAP	75	(6%)
Hemochromatosis	52	(4%)

Table II. Five most common adult onset conditions chosen, including discarded essays.

Across all essays, students were almost evenly split on whether they agreed or disagreed with the ASHG recommendation to defer testing until adulthood, as depicted in Table III.

Total Essays = 1241		
Testing Choice		
Defer	572	(46%)
Not Defer	554	(45%)
None	58	(5%)
Other	57	(5%)

Table III. Testing decision breakdown across all essays.

A statistically significant association was seen between which condition the student chose to discuss and whether or not the student supported deferring genetic testing ($p<.01$). While 64.4% of the students who submitted AD essays were in favor of deferring testing, only 46.1% of the students who submitted BRCA essays were in favor of deferring testing. Similarly, more BRCA essays supported not deferring testing (53.9%) than AD essays (35.6%) (Table IV). No association was found between sex or grade and the decision to defer or not defer in the comparison of BRCA and AD essays (Appendix A).

Defer vs. Not Defer for Alzheimer's and BRCA				
		Alzheimer's	BRCA	Total
Defer	Count	67	83	150
	%	64.4%	46.1%	52.8%
Not Defer	Count	37	97	134
	%	35.6%	53.9%	47.2%
Total	Count	104	180	284
	%	100.0%	100.0 %	100.0%

Chi-square (1) = 8.87, p<.01

Table IV. Chi square table showing percentage breakdown between defer and not defer in Alzheimer's and BRCA essays. Chi-square (1) value was found to be 8.87 with a p value of <.01, making the difference between the condition chosen and whether or not to defer significant.

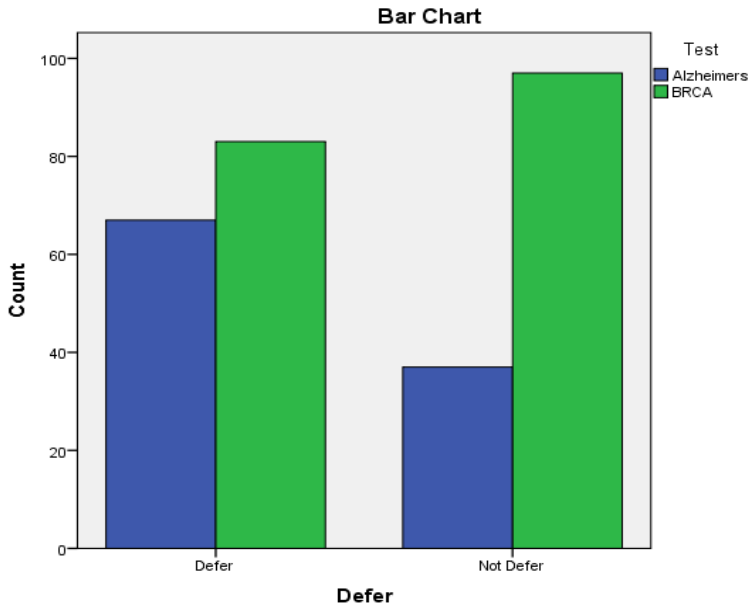

Figure 2. Bar graph depicting the number of defers and not defers in Alzheimer's and BRCA essays. Green bars represent BRCA essay choices while blue bars represent Alzheimer's essay choices.

AD and BRCA essays were examined for correlations between students' choices to defer or not defer. Table V and VI include the five most commonly used codes and their counter code. The top three most commonly used codes were examined for the purpose of extracting thematic quotes.

BRCA Thematic Categories	All	Defer	Not Defer
Psychological benefits to minor	78	8	67
Psychological risks to minor	248	179	53
Genetic testing variability and uncertain predictability	202	144	53
Genetic testing accuracy and predictability	19	9	10
Medical benefit/prevention	239	41	185
No medical benefit/not preventable	78	65	5
Mature and capable	24	1	23
Immature and incapable	73	63	7
Necessary to plan/prepare	100	10	86
Unnecessary to plan/prepare	13	12	1

Table V. Top five commonly used codes and their counter code within BRCA essays. Note: the defer and not defer columns do not add up to the total because there were None/Other essays included in the "all" column.

Alzheimer's Thematic Categories	All	Defer	Not Defer
Psychological benefits to minor	31	6	21
Psychological risks to minor	133	107	16
Genetic testing variability and uncertain predictability	162	125	26
Genetic testing accuracy and predictability	3	3	0
Medical benefit/prevention	66	15	47
No medical benefit/not preventable	68	59	6
Mature and capable	12	0	10
Immature and incapable	26	25	0
Necessary to plan/prepare	56	9	44
Unnecessary to plan/prepare	7	7	0

Table VI. Top five commonly used codes and their counter code within AD essays. Note: the defer and not defer columns do not add up to the total because there were None/Other essays included in the all column.

For the BRCA essay submissions that chose to defer, statements under the codes 'psychological risks,' 'genetic testing variability and uncertain predictability,' and 'no medical benefit or prevention' were mentioned the most. Those who chose to not defer discussed 'medical benefit and prevention,' 'necessary to plan or prepare,' and 'psychological benefits' the most. In two of the six most common codes applied to the defer and not defer essays there was a direct contrast: while the defer essays discussed 'psychological risks' and 'no medical benefit or prevention,' the not defer essays discussed 'psychological benefits' and 'medical benefit or prevention' (Table VII.).

Essay Totals (189)	**BRCA's Top Codes** (Number of times code was found within the essays)		
Defer (83)	Psychological Risks (179)	Genetic Testing Variability and Uncertain Predictability (144)	No Medical Benefit or Prevention (65)
Not Defer (97)	Medical Benefit and Prevention (185)	Necessary to Plan or Prepare (86)	Psychological Benefits (67)

Table VII. Top three codes represented in BRCA essays in the decision to defer or not defer.

In the AD student essays that chose to defer, the most commonly discussed reasons were 'genetic testing variability and uncertain predictability,' 'psychological risk,' and 'no medical benefit or prevention.' Those who chose to not defer most frequently discussed 'medical benefit and prevention,' 'necessary to plan or prepare,' and 'genetic testing variability and uncertain predictability.' Two of the codes applied to the defer and not defer essays directly contrasted with one another: 'no medical benefit or prevention' with defer and 'medical benefit and prevention' with not defer, while the code 'genetic testing variability and uncertain predictability' was used for both (Table VIII.).

Essay Totals (111)	Alzheimer's Top Codes (Number of times code was found within the essays)		
Defer (67)	Genetic Testing Variability and Uncertain Predictability (125)	Psychological Risks (107)	No Medical Benefit or Prevention (59)
Not Defer (37)	Medical Benefit and Prevention (47)	Necessary to Plan or Prepare (44)	Genetic Testing Variability and Uncertain Predictability (26)

Table VIII. Top three codes represented in AD essays in the decision to defer or not defer.

In both BRCA and AD essays the decision to defer was most commonly associated with the same three codes, although the order of the most common and second most common codes was reversed. The decision to not defer had the same top two codes in the same order ('medical benefit and prevention' and 'necessary to plan or prepare'); however, the third most used code for the decision to not defer was not shared between the two conditions ('psychological benefit' versus 'genetic testing variability and uncertain predictability'). Of note, because there were fewer essays discussing AD than BRCA, the codes were applied fewer times overall.

There was no association found between the number of times a code was applied and a student's sex or grade. All of the essays contained the code 'factual genetic/disorder information.' A complete list of correlations can be found in Appendix A.

DISCUSSION

There were several limitations of this study. Notably, this is not a representative sample of adolescents: only 1241 essays were submitted, six states did not submit any essays, 67% of the essays were submitted by females, and the majority of essays analyzed were from

the United States (87%). It is unclear whether the essay prompt was assigned to the entire class or if only the students who had the motivation to write an essay for the contest entered their submissions. In addition, teachers may have hand selected what they believed were the best essays to submit. Moreover, only two conditions were analyzed thematically, and these two conditions combined only make up half of the essays submitted. It is possible that upon further analysis of all essays, different codes could be emphasized.

The data gathered from these essays suggests that minors are insightful about predictive testing for adult onset conditions when given an outlet to express their opinions. Upon initial analysis, it seemed that the choice to defer or not defer was almost evenly split. However, when examined more thoroughly, their views on deferral were more complex and appeared to depend on the condition they chose. It is possible that upon learning about the ASHG position statement, students were inclined to inherently agree with a medical recommendation, regardless of the disease they chose. Another possibility is that a student's initial opinion concerning genetic testing of minors influenced the condition chosen. Additional qualitative analysis helped to identify possible reasons why these disease-specific themes emerged.

Defer Essay Themes

Students who chose to defer testing often cited the same reasons discussed in the clinical guidelines. One such theme that presents in both the BRCA and AD essays is 'psychological risks.' One student discussing the psychological risks of deferring BRCA testing stated, "*Overall, adolescents should not be tested for genetic diseases because of the emotional trauma that it can inflict on the person*" (Essay 1128, BRCA, Defer).

It is apparent that when weighing whether or not to defer testing, minors consider the emotional and psychological implications of genetic testing. This was noted in an AD essay in which a student states, "*Because there is no cure and limited treatment for Alzheimer's disease, oftentimes predictive genetic testing leads to depression and psychological problems*" (Essay 1105, AD, Defer). The potential adverse psychological outcomes that coincide with a positive genetic test result are clearly recognized by students and used to defend their stance on deferring testing.

Even for conditions that have medical management options, 'no medical benefit or prevention' was chosen as a top code to defer because the disease does not occur until adulthood. "*In the case of breast and ovarian cancers caused by BRCA mutations, there are preventative measures…However, since cancer does not appear until adulthood- the average age of diagnosis is 42 for breast and 52 for ovarian cancers (Brose et al, 2002)- this does not apply to adolescents*," as one student wrote (Essay 141, BRCA, Defer). This expresses the idea that minors may defer testing based on the absence of immediate medical benefit, a notion also included in the ASHG guidelines.

The final most commonly used reason for deferring testing was the variable and unpredictable nature of genetic testing. An AD student's essay states, "*It is important to note that having the APOE e4 allele does not cause the disease; the presence of the e4 allele is only one of the many factors that increase risk of development. Currently, no definitive test exists for the discovery of Alzheimer's disease in a living individual; the only conclusive test is an autopsy*" (Essay 5, AD, defer). Similarly, a student who chose BRCA argued, "*A positive test result does not mean that a person will definitely develop the cancers, it only indicates that the person has an increased risk*" (Essay 934, BRCA, Defer). Because there is

no straightforward genetic testing result for AD and BRCA, many students suggested that it would not be beneficial to get genetic testing as a minor. This argument is not mentioned in ASHG's position statement, but it seems to be important to minors.

BRCA and AD defer essays had the same three most common codes. Despite evidence that the reasons behind their decision to defer were similar, there were significantly more students who chose to defer testing for AD than BRCA. A possible reason for this finding may be due to the lack of medical surveillance and management options for Alzheimer's disease. By comparison, if someone is found to carry a BRCA mutation, there is medical management available; individuals could increase their cancer screening and consider prophylactic options. For AD, there are only clinical trials in place as a possible way to slow progression of the disease.

Not Defer Essay Themes

The top two codes used in support of not deferring testing were 'medical benefit' and 'genetic testing variability and uncertain predictability.' These codes were the same in both BRCA and AD essays. An example of the most common argument states that, "*adolescents should be encouraged to receive genetic testing if there is a chance they may have the BRCA1 or BRCA2 mutations to give them a chance to receive medical care to help prevent the development of breast or ovarian cancer in the future*" (Essay 1101, BRCA, Not Defer). When considering AD, one student wrote, "*I believe genetic testing is a positive way to find new things out about a certain disorder or mutation in DNA. You should take the opportunity of having a test done to prepare yourself for the future to live out a healthier and more preventative lifestyle*" (Essay 868, AD, Not Defer), demonstrating that there are perceived

medical benefits to early testing.

The third most common code noted in association with the decision to not defer testing in AD essays was particularly interesting and unexpected. Students mentioned 'genetic testing variability and uncertain predictability' third most despite deciding to not defer testing. This may indicate that even though students opted to proceed with testing, they found the genetic testing to be uncertain. Possible reasons they decided to not defer despite uncertainty in genetic testing were because they found the reasons to have genetic testing stronger than the unpredictability of the test. One student relates a version of this idea by saying, "*It should be encouraged for adolescents to take predictive or pre-dispositional testing...They need to be prepared for the reality that they indeed have the mutant gene however that does not mean that they are certainly going to get the illness*" (Essay 216, AD, Not Defer). Another student's argument supports this idea by saying, "*Researchers believe genetic testing will never be able to predict the disease with 100 percent accuracy due to environmental factors (The Genetics of Disease). Many people find this new technique to ease their anticipation that results from the unknown possibility of developing a fatal disease*" (Essay 499, AD, Not Defer).

Another reason that 'genetic testing variability and uncertain predictability' was used repeatedly may be due to the essay prompt itself. The prompt explicitly instructs students to "describe how the test works and how certain the test results are." While researching a condition, information on genetic testing uncertainty is readily available. It is likely that students included the uncertainty and variable predictability of genetic testing because it was required to discuss this aspect of their chosen genetic condition.

Conclusions

To help evaluate predictive testing on an individual level, genetic counselors should play an integral role in explaining the testing options, granting autonomy to the person pursuing testing. The theme of protecting autonomy was at the forefront of the national guidelines. The option to pursue genetic testing is important to minors too. As one student describes, "*I disagree with The American Society of Human Genetics' position statement. It should be encouraged for adolescents to take predictive or pre-dispositional testing. However a requirement should be that the teenager must see a genetics counselor who can explain to them exactly what it means to get tested and all of the possible outcomes*" (Essay 216, AD, Not Defer). This emphasizes the idea presented by HGSA that states a genetic test should be considered as an option on the basis of maturity instead of age after a psychosocial assessment.

It is clear from our analysis of the student essays that adolescents have well-formed opinions and insights about predictive genetic testing for adult onset conditions. Current guidelines acknowledge some flexibility on the issue of testing a minor; however, this flexibility is limited. Minors have shown that their standpoint on this matter is exceedingly individual and varies from person to person. Guidelines must acknowledge that minors' opinions are individualized. As an essential piece of the testing process, guidelines should recognize that adolescent perspectives are an integral factor when deciding whether or not to offer genetic testing to for adult onset conditions. It may be beneficial to implement more progressive guidelines reflecting this notion by considering each minor capable of assent on a case-by-case basis.

REFERENCES

Aatre, R. D., Mac, MS, & Day, S. M., MD, MPH (2001). Psychological Issues in Genetic Testing for Inherited Cardiovascular Diseases. *Circulation: Cardiovascular Genetics*, 4, 81-90.

American Academy of Pediatrics: Policy Statement (2013). Ethical and Policy Issues in Genetic Testing and Screening of Children. *Pediatrics,* 131(3). Retrieved February 22, 2017, from http://pediatrics.aappublications.org/content/131/3/620

American Society of Human Genetics Board of Directors & The American College of Medical Genetics Board of Directors (1995). Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents. *American Journal of Human Genetics*, 57, 1233-1241.

Anderson, J. A., Hayeems, R. Z., Shuman, C., Szego, M. J., Monfared, N., Bowdin, S., Meyn, M. S. (2015). Predictive genetic testing for adult-onset disorders in minors: A critical analysis of the arguments for and against the 2013 ACMG guidelines. *Clinical Genetics*, 87(4), 301–310. http://doi.org/10.1111/cge.12460

Borry, P., Stultiens, L., Nys, H., Cassiman, J. J., & Dierickx, K. (2006). Presymptomatic and predictive genetic testing in minors: A systematic review of guidelines and position papers. *Clinical Genetics*, 70(5), 374-381.

Botkin, J. R., Belmont, J. W., Berg, J. S., Berkman, B. E., Bombard, Y., Holm, I. A., Levy, H. P., Ormond, K. E., Saal, H. M., Spinner,N. B., Wilfond, B. S., & McInerney, J. D. (2015). Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents. *The American Journal of Human Genetics*, 97(1), 6-21.

Bradbury, A. R., Patrick-Miller, L., Ibe, C. N., Cummings, S. A., Olopade, O. I., & Daugherty, C. K. (2008). Should Genetic Testing for BRCA1/2 Be Permitted for Minors? Opinions of BRCA Mutation Carriers and Their Adult Offspring. *American Journal of Human Genetics Part C (Seminars in Medical Genetics)*, 148C, 70-77.

Bredenord, A. L., De Vries, M. C., & Van Delden, H. (2014). The Right to an Open Future Concerning Genetic Information. *The American Journal of Bioethics*, 14(3), 21-23.

Canadian Paediatric Society (2003). Guidelines for Genetic Testing of Healthy Children. *Paediatrics & Child Health*, 8(1), 42-45.

Duncan, R. E., & Delatycki, M. B. (2006). Predictive genetic testing in young people for adult-onset conditions: Where is the empirical evidence? *Clinical Genetics*, 69(1), 8–16. http://doi.org/10.1111/j.1399-0004.2005.00505.

Duncan, R., Gillam, L., Savulescu, J., Williamson, R., Rogers, J., & Delatycki, M. B. (2008). "You're One of Us Now": Young People Describe Their Experiences of Predictive Genetic Testing for HD and FAP. *American Journal of Medical Genetics*, *5*(2), 167–168. http://doi.org/10.1002/ajmg.c

European Society of Human Genetics (2009). Genetic testing in asymptomatic minors: Recommendations of the European Society of Human Genetics. *European Journal of Human Genetics,* 1-2. doi:10.1038/ejhg.2009.26

Friedman Ross, L., MD, PhD, Saal, H. M., MD, MPH, David, K. L., MD, MS, & Anderson, R. R., JD, MS. (2013). Technical report: Ethical and policy issues in genetic testing and screening of children. *Genetics in Medicine,* 15(3), 234-245.

Human Genetics Society of Australasia (2014). Guideline: Pre-symptomatic and Predictive Testing for Children

and Young Adults, 1-10. Retrieved May 26, 2016. https://www.hgsa.org.au/documents/item/272

Mand, C., Gillam, L., Delatycki, M. B., & Duncan, R. E. (2012). Predictive genetic testing in minors for late-onset conditions: a chronological and analytical review of the ethical arguments. *Journal of Medical Ethics*, 38(9), 519–524. http://doi.org/10.1136/medethics-2011-100055

Michie, S., Bobrow, M., & Marteau, T. M. (2001). Predictive genetic testing in children and adults: A study of emotional impact. *Journal of Medical Genetics*, 38, 519-526.

National Society of Genetic Counselors: Position Statement: Genetic Testing of Minors for Adult-Onset Conditions (2017). Retrieved February 22, 2017, from http://www.nsgc.org/p/bl/et/blogaid=860

Rhodes, R. (2006). Why test children for adult-onset genetic diseases? *The Mount Sinai Journal of Medicine, New York*, 73(3), 609–616.

Roberts, J. S., PhD, Cupples, A., PhD, Relkin, N. R., MD, PhD, Whitehouse, P. J., MD, PhD, & Green, R. C., MD, MPH. (2005). Genetic Risk Assessment for Adult Children of People With Alzheimer's Disease: The Risk Evaluation and Education for Alzheimer's Disease (REVEAL) Study. *Journal of Geriatric Psychiatry and Neurology*, 18(250), 250-255.

Wertz, Dorthy C., PHD, Fanos, Joanna H., PhD, Reily, Philip R., MD. (1994). Genetic Testing for Children and Adolescents. *The Journal of the Americal Medical Association*, 272(11), 875–881.

Appendix A

BRCA	ALL	Defer	Not Defe	Other/Non	Defer 9t	Defer 10t	Defer 11t	Defer 12t	Female Defe	Female Not defe	Male Defe	Male Not defe	Not Defer 9t	Not Defer 10t	Not Defer 11t	Not Defer 12t
1. Psychological benefits to minor	78	8	67	3	0	3	1	4	3	53	5	14	5	23	18	20
2. Psychological risks to minor	248	179	53	16	5	51	71	52	142	44	37	9	3	19	17	13
3. Genetic testing variability and uncertain predictability	202	144	53	5	1	46	54	43	120	46	24	7	5	15	14	18
4. Genetic testing accuracy and predictability	19	9	10	0	4	1	2	2	7	9	2	1	0	6	2	2
5. Factual genetic/disorder information	372	160	192	20	5	47	54	54	122	152	38	40	15	51	39	66
6. Incorrect facts	39	26	11	2	1	14	6	5	19	10	7	1	1	1	6	3
7. Risks to family	38	31	6	1	0	9	13	9	26	5	5	1	0	1	4	1
8. Benefits to family	27	5	22	0	0	3	2	0	3	15	2	7	2	10	1	7
9. Personal experience with the condition	15	5	9	1	0	0	2	3	3	8	2	1	1	0	3	5
10. Personal experience with testing	11	4	7	0	0	0	3	1	3	7	1	0	1	0	1	5
11. Medical benefit/prevention	239	41	185	13	1	11	16	13	38	144	3	41	15	39	44	65
12. No medical benefit/not preventable	78	65	5	8	3	15	16	31	52	4	13	1	0	3	1	2
13. Disrupts formative years	60	49	9	2	2	14	10	23	39	8	10	1	2	0	4	6
14. Social risks	24	19	0	5	1	10	4	4	14	0	5	0	0	0	0	0
15. Social benefits	2	0	2	0	0	0	0	0	0	2	0	0	0	0	1	1
16. Mature and capable	24	1	23	0	0	0	1	0	1	21	0	2	0	5	12	6
17. Immature and incapable	73	63	7	3	3	23	20	17	46	6	17	1	1	0	5	2
18. Potential discrimination	21	16	3	2	1	6	2	7	10	2	6	1	0	0	1	2
19. Necessary to plan/prepare	100	10	86	4	0	5	4	1	9	71	1	15	10	25	29	21
20. Unecessary to plan/prepare	13	12	1	0	0	2	7	3	9	1	3	0	0	1	0	0
21. Advancements in science	16	5	11	0	0	2	3	0	3	10	2	1	2	2	6	1
22. Case-by-case	8	4	4	0	0	1	3	0	3	3	1	1	1	0	0	3
23. Loss of autonomy	21	16	4	1	0	5	5	6	14	4	2	0	0	0	2	3
24. Individual's choice	51	6	38	7	0	1	1	4	6	34	0	4	2	10	21	5
25. Family/parent's choice	21	2	16	3	0	2	0	0	1	12	1	4	0	14	2	0

Appendix I: Complete list of codes and frequency of use in BRCA essays.

Alzheimer's	ALL	Defer	Not Defer	Other/None	Defer 9th	Defer 10th	Defer 11th	Defer 12th	Female Defer	Female Not Defer	Male Defer	Male Not Defer	Not Defer 9th	Not Defer 10th	Not Defer 11th	Not Defer 12th
1. Psychological benefits to minor	31	6	21	4	0	1	1	4	5	20	1	1	1	7	9	4
2. Psychological risks to minor	133	107	16	10	15	22	20	25	89	15	18	1	3	5	5	3
3. Genetic testing variability and uncertain predictability	162	125	26	11	12	30	23	32	114	25	11	1	1	12	5	8
4. Genetic testing accuracy and predictability	3	3	0	0	0	0	1	2	3	0	0	0	0	0	0	0
5. Factual genetic/disorder information	204	125	66	13	18	23	24	41	107	53	18	13	6	27	21	12
6. Incorrect facts	11	6	4	1	2	1	0	3	4	4	2	0	1	0	3	0
7. Risks to family	24	23	0	1	5	4	7	5	20	0	3	0	0	0	0	0
8. Benefits to family	6	1	5	0	0	0	0	1	1	3	0	2	0	4	1	0
9. Personal experience with the condition	20	11	8	1	0	0	4	4	10	7	1	1	0	2	3	3
10. Personal experience with testing	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0
11. Medical benefit/prevention	66	15	47	4	1	3	5	3	15	41	0	6	9	15	16	7
12. No medical benefit,/not preventable	68	59	6	3	5	20	8	9	55	6	4	0	0	2	2	2
13. Disrupts formative years	29	25	3	1	3	6	3	11	21	3	4	0	1	2	0	0
14. Social risks	9	7	1	1	2	1	1	3	5	1	2	0	0	1	0	0
15. Social benefits	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16. Mature and capable	12	0	10	2	0	0	0	0	0	9	0	1	0	2	1	7
17. Immature and incapable	26	25	0	1	2	1	8	7	21	0	4	0	0	0	0	0
18. Potential discrimination	20	19	1	0	1	4	7	4	15	1	4	0	0	0	0	1
19. Necessary to plan/prepare	56	9	44	3	2	0	3	4	9	36	0	8	4	17	12	11
20. Unecessary to plan/prepare	7	7	0	0	1	0	2	2	7	0	0	0	0	0	0	0
21. Advancements in science	22	6	16	0	0	1	4	1	6	13	0	3	0	6	10	0
22. Case-by-case	3	0	2	1	0	0	0	0	0	2	0	0	0	0	0	2
23. Loss of autonomy	10	8	1	1	0	3	2	2	8	1	0	0	0	0	0	1
24. Individual's choice	19	4	9	6	1	0	0	3	4	9	0	0	4	1	0	4
25. Family/parent's choice	2	0	1	1	0	0	0	0	0	1	0	0	0	1	0	0

Appendix II: Complete list of codes and frequency of use in Alzheimer's essays.